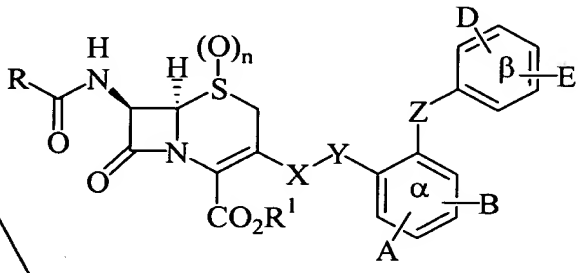
CLAIMS

We claim:

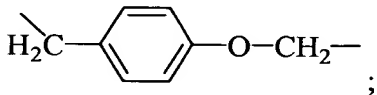
1. A compound of the following structure:



wherein n is 0, 1 or 2;

wherein A, B, D, and E are independently the same, different or absent and are selected from the group consisting of a halogen, H, CN, NO_2, CF_3, C(O)H, NH_2, $N(R^2)_{n1}$, and $C(O)CH_3$, OR^2, wherein R^2 is selected from the group consisting of H, lower alkyl, alkenyl group, and alkynyl group and wherein n1 is 0, 1 or 2;

wherein X is selected from the group consisting of CH_2, *cis*-CH=CH-CH_2-, *trans*-CH=CH-CH_2, -CH_2-O-C(O)-, -NH-C(O)-O-, —C≡C—CH_2, -PO_3-, -SO_3-, -SO_2, -NH-CH_2-CH_2-CH_2-NH-CO-, traceless Linker, and

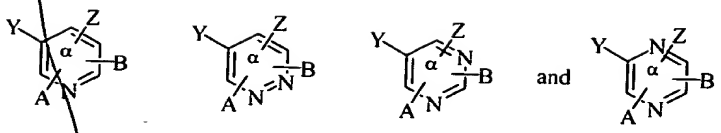


;

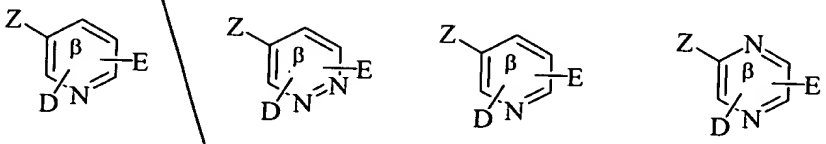
wherein Y is selected from the group consisting of -O-, -S-, and NR^3, wherein R^3 is selected from the group consisting of H, lower alkyl, alkenyl group, and alkynyl group;

wherein Z is selected from the group consisting of -O-, -C(O)-, -S-, α-C(O)-$N(R^4)$-β, α-$N(R^4)$-C(O)-β, and $N(R^4)_{n2}$, wherein R^4 is selected from the group consisting of H, OH, R^5, and OR^5, wherein R^5 is selected from the group consisting of H, lower alkyl, alkenyl group, and alkynyl group and wherein n2 is 0, 1 or 2;

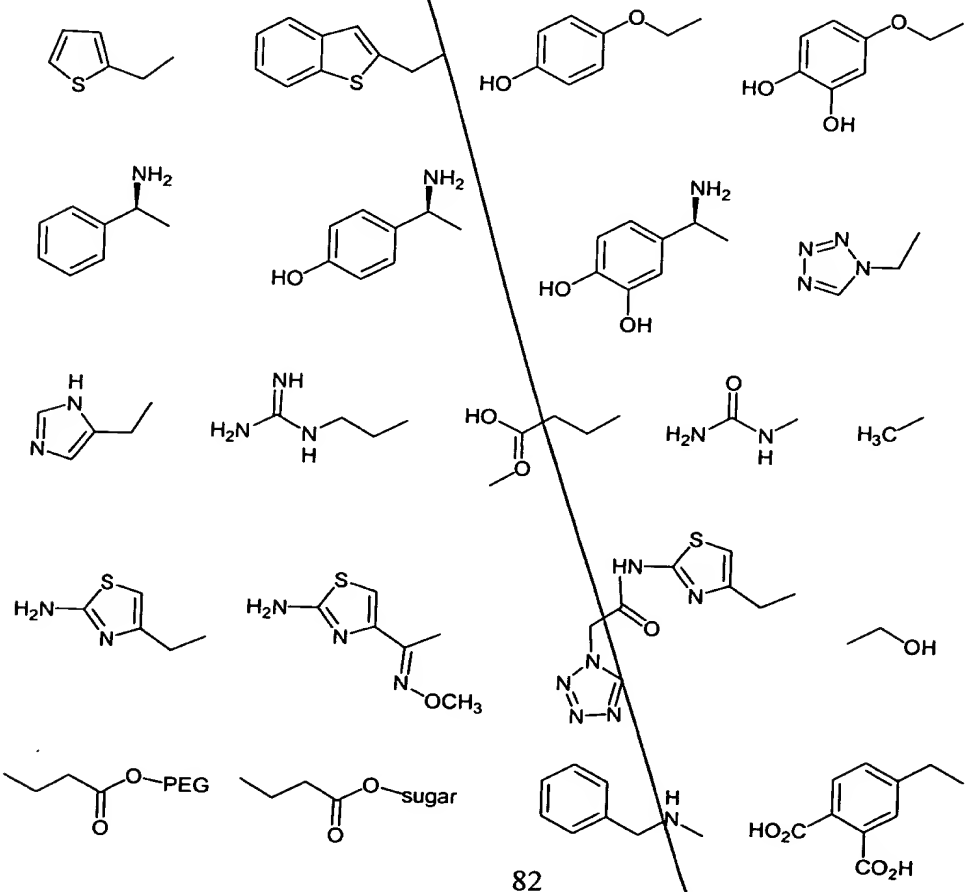
wherein ring α connects Y to Z and is a benzene or a heterocycle selected from the group consisting of



wherein ring β connects to Z and is a benzene or a heterocycle selected from the group consisting of



wherein R is selected from the group consisting of Ph-, $PhCH_2$- and $PhOCH_2$; or a structure selected from:



Sub A2

wherein R^1 is selected from the group consisting of H, Li, Na, sugar, THAM (2-amino-2-hydroxymethyl-1,3-propanediol), ammonium, methylamine, dimethylamine, lower alkylamine, bis(lower alkyl)amine and polyethylene glycol (PEG); and derivatives and pharmaceutically acceptable salts of the compounds.

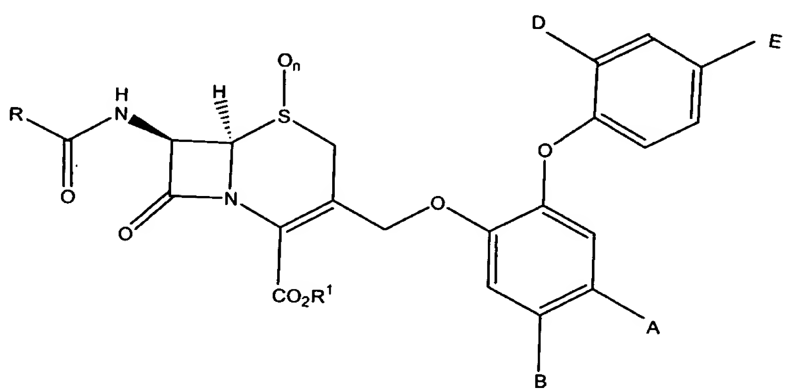
2. The compound of claim 1, wherein n is 0 or 1.

3. The compound of claim 2, wherein X is $-CH_2-$.

4. The compound of claim 3, wherein Y is O.

5. The compound of claim 4, wherein Z is O.

6. The compound of claim 5, wherein the compound has the following structure:

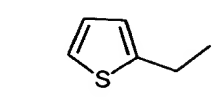
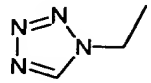
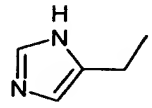
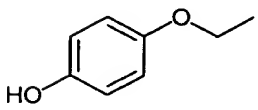
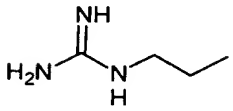
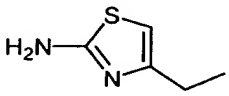
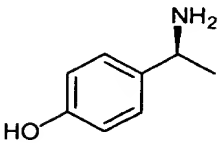
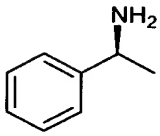
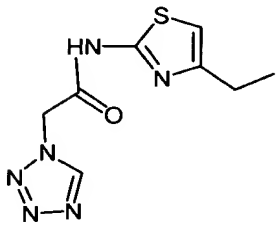


7. The compound of claim 6, wherein B, D and E are each halogens.

8. The compound of claim 7, wherein B, D and E are Cl.

9. The compound of claim 8, wherein A is hydrogen.

10. The compound of claim 9, wherein R is selected from the group consisting of









and


11. The compound of claim 10, wherein R^1 is hydrogen.

12. The compound of claim 11, wherein n is 0.

13.The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-3-cephem-4-carboxylic acid (Compound 9).

14.The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(1-tetrazoleacetamido)-3-cephem-4-carboxylic acid (Compound 29).

15. The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-[2-(3*H*-imidazol-4-yl)]-acetamido-3-cephem-4-carboxylic acid (Compound 31).

16. The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(1-phenyl-2-aminoacetamido)-3-cephem-4-carboxylic acid (Compound 38).

17. The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-[4-(2-aminothiazole)-yl-2-acetamido]-3-cephem-4-carboxylic acid (Compound 39).

18. The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-[2-(4-hydroxyphenoxy)acetamido]-3-cephem-4-carboxylic acid (Compound 40).

19. The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-[2-amino-2-(4-hydroxy-phenyl)acetamido)-3-cephem-4-carboxylic acid (Compound 41).

20. The compound of claim 12, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(3-guanidinopropyl)acetamido-3-cephem-4-carboxylic acid (Compound 42).

21. The compound of claim 12, wherein the compound is 3-[5-chloro-2-(2,4-dichlorophenoxy)-phenoxymethyl]-7-{2-[2-(2-tetrazol-1-yl-acetamido)-thiazol-5-yl]-acetamido-3-cephem-4-carboxylic acid (Compound 43).

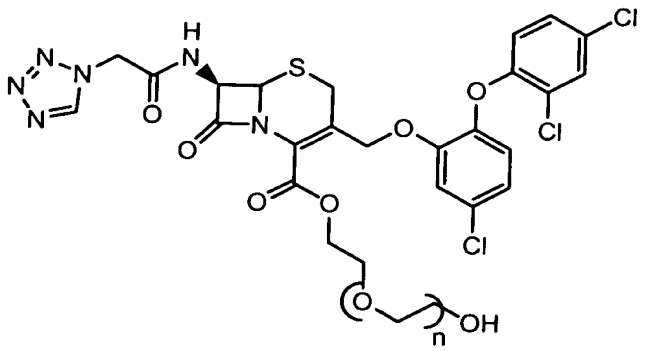
22. The compound of claim 11, wherein n is 1.

23. The compound of claim 22, wherein the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-1-oxo-3-cephem-4-carboxylic acid (Compound 11).

24.The compound of claim 10, wherein R^1 is polyethylene glycol (PEG).

25. The compound of claim 24, wherein n is 0.

26. The compound of claim 25, wherein the compound has the following structure:



wherein n is 4 to 2000. (Compound 32)

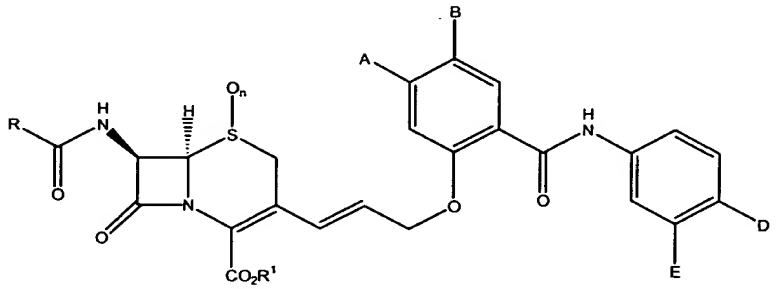
27. The compound of claim 2, wherein X is cis–CH=CH-CH_2- or trans–CH=CH-CH_2.

28. The compound of claim 27, wherein Y is O.

29. The compound of claim 28, wherein Z is α-C(O)-N(R^4)-β.

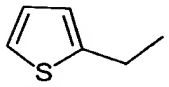
30. The compound of claim 29, wherein R^4 is hydrogen.

31. The compound of claim 30, wherein the compound has the following structure:



32. The compound of claim 31, wherein R^1 is hydrogen.

33. The compound of claim 32, wherein R is



34. The compound of claim 33, wherein B, D, and E each halogens.

35. The compound of claim 34, wherein B, D and E are Cl.

36. The compound of claim 35, wherein A is hydrogen.

37. The compound of claim 36, wherein n is 0.

38. The compound of claim 37, wherein the compound is 3-{3-[4-chloro-2-(3,4-dichloro-phenylcarbamoyl)-phenoxy]-propenyl}-7-(2-thiophene-acetmido)-3-cephem-4-carboxylic acid (Compound 35).

39. A composition comprising the compounds of claim 1 and a carrier.

40. The composition of claim 39, wherein the carrier is a pharmaceutically acceptable carrier.

41. A method of inhibiting the growth of a microorganism comprising contacting the microorganism with an effective amount of the compound of claim 1.

42. The method of claim 41, wherein the microorganism expresses β-lactamase.

43. The method of claim 42, wherein the microorganism is selected from the group consisting of *Staphylococcus aureus, Staphylococcus epidermidis* and other coagulase-negative staphylococci, *Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, Enterococcus* species, *Corynebacterium diphtheriae, Listeria monocytogenes, Bacillus anthracis, Neisseria meningitidis, Neisseria gonorrhoeae, Moraxella catarrhalis, Vibrio cholerae, Campylobacter jejuni, Enterobacteriaceae* (includes: *Escherichia, Salmonella, Klebsiella, Enterobacter), Pseudomonas aeruginosa, Acinetobacter* species, *Haemophilus influenzae, Clostridium tetani, Clostridium botulinum, Bacteroides* species, *Prevotella* species, *Porphyromonas* species, *Fusobacterium* species, *Mycobacterium tuberculosis, and Mycobacterium leprae,*

with the proviso that when the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-3-cephem-4-carboxylic acid, the microorganism is not *Pseudomonas aeruginosa.*

44. The method of claim 41, wherein the microorganism is vancomycin resistant, tolerant or sensitive.

45. The method of claim 44, wherein the vancomycin resistant, tolerant or sensitive microorganism is selected from the group consisting of *Staphylococcus aureus, Staphylococcus epidermis, Enterococcus faecalis* and *Enterococcus faecium.*

46. A method for inhibiting penicillin binding protein in an infected cell comprising contacting the cell with an effective amount of claim 1.

47. The method of claim 46, wherein the infected cell is vancomycin resistant, tolerant or sensitive.

48. The method of claim 47, wherein the vancomycin resistant, tolerant or sensitive infected cell is selected from the group consisting of *Staphylococcus aureus, Staphylococcus epidermis, Enterococcus faecalis* and *Enterococcus faecium.*

49. A method for treating a subject infected with a microorganism, comprising administering to the subject an effective amount of the compound of claim 1, thereby treating the subject.

50. The method of claim 49, wherein the microorganism produces -lactamase.

51. The method of claim 50, wherein the microorganism is selected from the group consisting of *Staphylococcus aureus, Staphylococcus epidermidis* and other coagulase-negative staphylococci, *Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, Enterococcus* species, *Corynebacterium diphtheriae, Listeria monocytogenes, Bacillus anthracis, Neisseria meningitidis, Neisseria gonorrhoeae, Moraxella catarrhalis, Vibrio cholerae, Campylobacter jejuni, Enterobacteriaceae* (includes: *Escherichia, Salmonella, Klebsiella, Enterobacter), Pseudomonas aeruginosa, Acinetobacter* species, *Haemophilus influenzae, Clostridium tetani, Clostridium botulinum, Bacteroides* species, *Prevotella* species, *Porphyromonas* species, *Fusobacterium* species, *Mycobacterium tuberculosis, and Mycobacterium leprae,*

with the proviso that when the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-3-cephem-4-carboxylic acid, the microorganism is not *Pseudomonas aeruginosa.*

52. The method of claim 49, wherein the microorganism is vancomycin resistant, tolerant or sensitive.

53. The method of claim 52, wherein the vancomycin resistant, tolerant or sensitive microorganism is selected from the group consisting of *Staphylococcus aureus, Staphylococcus epidermis, Enterococcus faecalis* and *Enterococcus faecium.*

54. A method of screening for an antibacterial agent comprising contacting a sample containing a bacterial cell with a test agent and contacting a second sample containing the bacterial cell with a compound of claim 1 and comparing the ability of each to inhibit the growth of the bacterial cell.

55. The method of claim 54, wherein the bacterial cell produces β-lactamase.

56. The method of claim 55, wherein the bacterial cell is selected from the group consisting of *Staphylococcus aureus, Staphylococcus epidermidis* and other coagulase-negative staphylococci, *Streptococcus pyogenes, Streptococcus pneumoniae, Streptococcus agalactiae, Enterococcus* species, *Corynebacterium diphtheriae, Listeria monocytogenes, Bacillus anthracis, Neisseria meningitidis, Neisseria gonorrhoeae, Moraxella catarrhalis, Vibrio cholerae, Campylobacter jejuni, Enterobacteriaceae* (includes: *Escherichia, Salmonella, Klebsiella, Enterobacter), Pseudomonas aeruginosa, Acinetobacter* species, *Haemophilus*

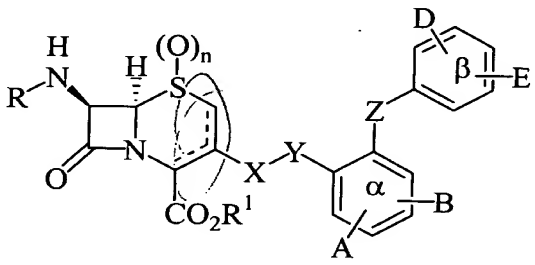
influenzae, Clostridium tetani, Clostridium botulinum, Bacteroides species, *Prevotella* species, *Porphyromonas* species, *Fusobacterium* species, *Mycobacterium tuberculosis, and Mycobacterium leprae,*

with the proviso that when the compound is 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-3-cephem-4-carboxylic acid, the bacteria is not *Pseudomonas aeruginosa.*

57. The method of claim 54, wherein the bacterial cell is vancomycin resistant, tolerant or sensitive.

58. The method of claim 57, wherein the vancomycin resistant, tolerant or sensitive bacterial cell is selected from the group consisting of *Staphylococcus aureus, Staphylococcus epidermis, Enterococcus faecalis* and *Enterococcus faecium.*

59. A compound of the following structure:



wherein n is 0 or 1;

wherein A, B, D, and E are independently the same, different or absent and are selected from the group consisting of a halogen, H, and NO_2;

wherein X is selected from the group consisting of CH_2, *cis*-CH=CH-CH_2-, *trans*-CH=CH-CH_2, and -CH_2-O-C(O)-;

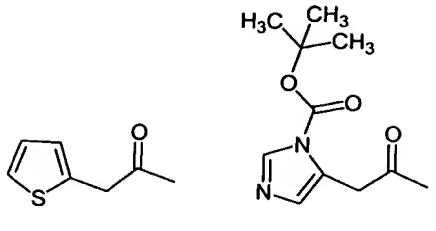
wherein Y is -O-;

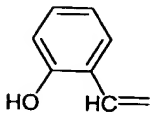
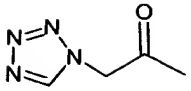
wherein Z is -O- or α-C(O)-N(H)-β or absent;

wherein ring α connects Y to Z and is a benzene;

wherein ring β connects to Z and is a benzene or is absent;

wherein R is selected from the group consisting of



and H;

and wherein R^1 is diphenylmethyl or 4-nitrobenzyl.

60. The compound of claim 59, wherein the compound is diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-3-cephem-4-carboxylate (Compound 7).

61. The compound of claim 59, wherein the compound is diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-2-cephem-4-carboxylate (Compound 8).

62. The compound of claim 59, wherein the compound is diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(2-thienylacetamido)-1-oxo-3-cephem-4-carboxylate (Compound 10).

63. The compound of claim 59, wherein the compound is diphenylmethyl 3-(4-nitrophenoxycarbonyloxy)methyl-7-(2-thienylacetamido)-3-cephem-4-carboxylate (Compound 12).

64. The compound of claim 59, wherein the compound is diphenylmethyl 3-((2-(2,4-dichlorophenoxy)-5-chlorophenoxy)carbonyloxy)methyl-7-(2-thienylacetamido)-2-cephem-4-carboxylate (Compound 14).

65. The compound of claim 59, wherein the compound is diphenylmethyl 3-((2-(2,4-dichlorophenoxy)-5-chlorophenoxy)carbonyloxy)methyl-7-(2-thienylacetamido)-3-cephem-4-carboxylate (Compound 13).

66. The compound of claim 59, wherein the compound is diphenylmethyl 3-((2-(2,4-dichlorophenoxy)-5-chlorophenoxy)carbonyloxy)methyl-7-(2-thienylacetamido)-1-oxo-3-cephem-4-carboxylate (Compound 16).

67. The compound of claim 59, wherein the compound is 4-nitrobenzyl 3-(1-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)-3-propenyl)-7-(2-thienylacetamido)-3-cephem-4-carboxylate (Compound 23).

68. The compound of claim 59, wherein the compound is diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-β-(o-hydroxy)benzylidenamino -3-cephem-4-carboxylate (Compound 26).

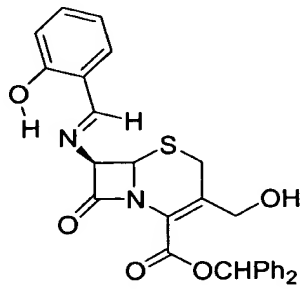
69. The compound of claim 59, wherein the compound is diphenylmethyl-3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-amino-3-cephem-4-carboxylate (Compound 27).

70. The compound of claim 59, wherein the compound is diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-(1-tetrazoleacetamido)-3-cephem-4-carboxylate (Compound 28).

71. The compound of claim 59, wherein the compound is diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-[2-(3-*tert*-butoxycarbonyl-3*H*-imidazol-4-yl)]-acetamido-3-cephem-4-carboxylate (Compound 30).

72. The compound of claim 59, wherein the compound is diphenylmethyl-3-{3-[4-chloro-2-(3,4-dichloro-phenylcarbamoyl)-phenoxy]-propenyl}-7-(2-thiophene-acetamido)-3-cephem-4-carboxylate (Compound 34).

73. A process for preparing diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-β-(o-hydroxy)benzylidenamino -3-cephem-4-carboxylate which comprises reacting an effective amount of a compound having the structure:



a) with an effective amount of triclosan and cooling;

b) adding an effective amount of triphenylphosphine;

c) adding an effective amount of diisopropylazodicarboxylate and combining with an aqueous solvent and extracting with ethylacetate; and

d) concentrating the compound, thereby preparing diphenylmethyl 3-(2-(2,4-dichlorophenoxy)-5-chlorophenoxy)methyl-7-β-(o-hydroxy)benzylidenamino -3-cephem-4-carboxylate.